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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/699,502	10/31/2003	Jiong Wu	SRCK:066 12642.0066.NPUS0	3578

23369 7590 01/04/2007

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EXAMINER	
HANLEY, SUSAN MARIE	
ART UNIT	**PAPER NUMBER**
1651	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	01/04/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/699,502	WU ET AL.	
	Examiner	Art Unit	
	Susan Hanley	1651	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *05 September 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-5,13-18,20 and 21* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-5, 13-18, 20 and 21* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

The amendment and remarks filed 9/5/06 are acknowledged.

Claims 1-5 and 13-21 are pending.

Response to Arguments

Applicant's arguments with respect to claims 1-5, 13-18, 20 and 21 have been considered but are moot in view of the new ground(s) of rejection over the amended claims.

Claim Rejections - 35 USC § 112

Claims 1-5, 13-18, 20 and 21 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a reagent system comprising a first reagent having:

a saponin;

an acid selected from the group consisting of phosphoric acid, a halogenated acid and a combination thereof;

and an additional surfactant that is not a saponin; wherein said first reagent has been autoclaved at 121 degrees C; and

and a second reagent comprising a quenching agent; and methods of use, thereof, for lysing RBC while stabilizing white blood cells and preparing whole blood samples for leukocyte analysis, does not reasonably provide enablement for a first reagent system comprising an autoclaved saponin and an acid selected from the group consisting of phosphoric acid, a halogenated acid and a combination thereof, and a quenching agent; and the methods of use thereof. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make or use the invention commensurate in scope with these claims.

The claims have been amended to a reagent system comprising an autoclaved saponin, an acid selected from phosphoric acid or a halogenated acid and a quenching agent, and methods of use thereof.

However, the only autoclaved saponin disclosed by the specification is a modified saponin composition comprising a saponin together with phosphoric acid or a halogenated acid and an additional surfactant that is not a saponin, wherein the entire composition is autoclaved by heating at 121 degrees. At page 5, lines 4-8, the specification discloses that, "Modified saponin derivatives are synthesized by heating at 121°C in solution containing chloroacetic acid and surfactant. Such saponin derivatives are significantly different from the original saponin. The modification allows (1) a much broader range of saponin derivative concentration, ranging from 0.020% - 0.035%, which can be used in the red blood cell lyse; and (2) a significantly longer stability for the reagents."

Therefore, it appears that the saponin, the acid and the surfactant must be present together for the autoclaving process which occurs at 121°C. It would appear that the presence of all three components are required for the autoclave-driven reaction at 121°C to make the claimed cell lysis reagent having the desired stability properties. This method of making the reagent is significantly different from a reagent system that comprises a saponin that is autoclaved and an acid. Chemical reactions require the reactants and activation energy necessary to make the desired product. The specification does not disclose if one skilled in the art can autoclave the saponin alone at any temperature without the acid and surfactant to obtain the hemolysis reagent comprising a heated saponin with the desired hemolytic characteristics and apparent special stability with a reasonable expectation of results.

Applicants point out that the saponin reagent kept at room temperature for up to 8 months loses its activity (p. 11). Hence, it is highly desirable obtain a stabilized saponin reagent. However, the specification shows one preparative method (heating at 121 degrees C for 30 min.) to obtain a product that is characterized as having as being more stable than the unheated product. It is noted from Dave et al. (2000) that an autoclaving process does not mean one precise temperature and pressure. Dave et al. show on page 203 an autoclaving temperature process can occur at a wide range of temperatures and pressures. The specification does not teach what combination of autoclave temperature and pressure, other than what is disclosed by the specification.

It appears that the stabilization imparted by the heating procedure is limited to a temperature of about 121 degree C to a compostion that contains at a minimum: a saponin, a haloacetic or phosphoric acid or a combination thereof and an additional surfactant that is not a saponin. Hence, one skilled in the art would be unable to pick a temperature and reaction conditions to provide a reagent system comprising the modified saponin disclosed by the specification and expect it to possess the same set of properties. If the heating method is not generally applicable to any possible temperature or the presence of an acid and surfactant, then the desired stabilization of the saponin would be considered individually. This would be considered undue experimentation.

There is no reliable method that predicts which temperature/reaction conditions produce the stabilized saponin specie that is described in the specification. The specification discloses that the stability of the autoclaved saponin/acid/non-saponin surfactant compostion is unexpected. However, the specification does not teach how one of ordinary skill in the art could decide *a priori* which reaction conditions/temperatures will provide a saponin with the desired characteristics. The limited disclosure cannot be extrapolated by the skilled artisan to predict which reaction conditions/temperatures other than autoclaving, at 121 degrees C, a composition comprising a saponin, a haloacetic or phosphoric acid and a non-saponin surfactant will produce a stabilized saponin with the desired stability and hemolytic activity. It would require one of ordinary skill in the art undue experimentation to determine what reaction conditions/temperatures other than those stated will produce a stabilized saponin according to the directions of the instant disclosure. Thus, claims 1-5, 13-18, 20 and 21 are not commensurate in scope with the enabling disclosure.

The citation of Dave et al. does not constitute new grounds of rejection because the citation was made in response to the amendment related to an autoclaved saponin.

Claims 5 and 14 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the

specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Claims 5 and 14 recite the new limitation regarding "mixing at a calculated ratio a saponin solution heated at about 121 degrees C for about 30 minutes and an unheated saponin solution...". The specification does not teach the claimed calculated ratios not how to calculate them. In view of the lack of disclosure and examples thereof, one of ordinary skill would not have considered the applicant to be in possession of the invention as filed and the additions to the claims are considered to be NEW MATTER.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 5 and 14 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 5 and 14 recite the new limitation regarding "mixing at a calculated ratio a saponin solution heated at .... and an unheated saponin solution...". This phrase is confusing because "a saponin solution" lacks antecedent basis in claims 1 and 13, respectively.

Allowable Subject Matter

A reagent system for a reagent system for lysing red blood cells comprising a first reagent having a saponin; an acid selected from the group consisting of phosphoric acid, a halogenated acid and a combination thereof; and an additional surfactant that is not a saponin; wherein said first reagent has been autoclaved at 121 degrees C; and a second reagent comprising a quenching agent; and methods of use, thereof, for lysing RBC while stabilizing white blood cells and preparing whole blood samples for leukocyte analysis are neither anticipated nor suggested by the prior art.

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL.** See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Susan Hanley whose telephone number is 571-272-2508. The examiner can normally be reached on M-F 9:00-5:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Wityshyn can be reached on 571-272-0926. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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